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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
077967,267	10/27/92	COOK	P ISIS-0710

12M1/1126

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EXAMINER
KUNZ, G

ART UNIT	PAPER NUMBER
1211	23

DATE MAILED: 11/26/96

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on Amendment D filed 8-19-96

☐ This action is FINAL.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire THREE month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 9-10 AND 15-27 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 9-10 AND 15-27 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 15, 17, 18

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

-- SEE OFFICE ACTION ON THE FOLLOWING PAGES --

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PTOL-326 (Rev. 10/95)

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Applicant's amendment D filed 8-19-96 has been received and entered into the record.

Claims 9 - 10 and 15 - 27 are pending in the case.

Any 35 USC statutes not cited in this Office action can be found cited in full in a previous Office action.

Claims 9 - 10 and 15 - 27 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 1 - 8, 62 - 63, and 69 - 72 of copending application SN 08/373,298. Applicant has requested that this issue be deferred until all of the other pending rejections have been withdrawn.

Claims 26 - 27 are rejected under 35 U.S.C. § 103 as being unpatentable over Buhr (5,466,786) for the reasons already of record on pages 3 - 5 of the Office action mailed 5-16-96. The applicant argues against this rejection on the grounds that the Buhr patent is not enabling for the preparations of 2'-O-modified guanosine derivatives because Sproat et al. and Inoue et al. indicate that guanosine is more difficult to alkylate than pyrimidine nucleosides. This argument has been fully considered but is not deemed persuasive. The applicant points out that Sproat et al. teaches in the first paragraph of the introduction that an alkylation procedure that was effective for alkylating 2'-OH of pyrimidine nucleosides could not be used effectively to alkylate guanosine. However, Sproat et al. then states that they

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have solved these problems by another synthetic route (last line of first paragraph). Similarly, Inoue et al. teaches in the abstract that methyl iodide was not very effective for the alkylation of guanosine, but that diazomethane proved to be a successful alternative (Abstract, first two sentences). While some of the synthetic routes to 2'-O-alkylated guanosine may not give high yields, for an obviousness rejection, all that this necessary is that prior art provide a method that yields some material, not an optimal yield.

Claims 9 - 10 and 15 - 27 are rejected under 35 U.S.C. § 103 as being unpatentable over Teoule et al. (WO 90/08156) in view of Kikuchi et al.

The claims are directed to 2'-O-modified guanosine or 2'-O-modified 2-aminoadenosine wherein the moiety attached to the 2'-O-position is alkyl(1 - 20 carbon atoms), alkenyl(2 - 20 carbon atoms, or alkynyl((2 - 20 carbon atoms) substituted by halogen, sulfone, N-alkyl, N-dialkyl, O-alkyl, etc.

Teoule et al. discloses a 2'-O-substituted nucleosides which are a linear or branched, substituted or unsubstituted hydrocarbon wherein the substituents are O, S, N, NHCO, NHSO₂, SO₂, CO, alkynyl, or alkenyl (claim 1 and page 4, lines 16 - 26). While Teoule et al. does not disclose 2-aminoadenosine, Kikuchi et al. does teach that the substitution of 2-aminoadenosine for adenosine results in increased hybridization strength.

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Therefore, it would have been obvious to the person of ordinary skill in the art to have substituted one of the modifications taught by Teoule et al. at the 2'-O-positions of guanosine or 2-aminoadenosine (disclosed by Kikuchi) for the purpose of preparing oligonucleotides having 1) increased melting temperature and 2) resistance to nuclease digestion. Thus, the invention is prima facie obvious in the absence of clear and convincing evidence to the contrary.

The substitution of a fluorine for a hydrogen on a carbon atoms of the above modifications is an obvious replacement because the atomic radius of fluorine and hydrogen are quite similar and the carbon-fluorine bond is quite stable.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Kunz, whose telephone number is (703) 308-4623. The examiner can normally be reached on Tuesday through Friday from 6:30 AM to 4:00 PM. The examiner can also be reached on alternate Mondays.

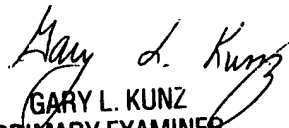
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John Kight, can be reached on (703) 308-0204. The fax phone number for this Group is (703) 308-4556.

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Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.


GARY L. KUNZ
PRIMARY EXAMINER
GROUP 1200

Gary L. Kunz, Ph.D.
November 25, 1996